61. (New) The oligonucleotide of claim 26, wherein the oligonucleotide comprises SEQ ID NO:19.

62. (New) The oligonucleotide of claim 26, wherein the oligonucleotide comprises SEQ ID NO:20.

63. (New) An *in vitro* method for inhibiting expression of tenascin by a cell, said method comprising exposing said cell to an oligonucleotide comprising a sequence selected from SEQ ID NO. 2, SEQ ID NO. 3, SEQ ID NO. 4, SEQ ID NO. 5, SEQ ID NO. 6, SEQ ID NO. 7, SEQ ID NO. 8, SEQ ID NO. 9, SEQ ID NO. 10, SEQ ID NO. 11, SEQ ID NO. 12, SEQ ID NO. 13, SEQ ID NO. 14, SEQ ID NO. 15, SEQ ID NO. 16, SEQ ID NO. 17, SEQ ID NO. 19, and SEQ ID NO. 20.

## REMARKS

By this Amendment, claims 24, 25, and 36-40 are cancelled, claims 26, 27, 32, 33, and 42-44 are amended, and new claims 45-63 are entered. Support for the amendments to claims 26, 27, 32, 33, and 42-44, and for new claims 45-63, comes from the specification and claims, as originally filed, for example at page 3, lines 1-9, and page 5. Accordingly, no new matter is added by this Amendment. Currently, claims 26-35 and 41-63 are pending in this application.

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I. *Rejection Under 35 U.S.C. § 112, first paragraph*

A. Written Description

The Office maintains the rejection of claims 24-44 under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description of the claimed oligonucleotides. (Final Office Action at pages 2-3.) Applicants respectfully traverse this rejection as it applies to rejected claims 26-35 and 41-44, and as it might be applied to new claims 45-63.

Applicants respectfully submit that the presently claimed oligonucleotides and method are fully described in the present specification at pages 5, 12, and 14, and in the Examples. Accordingly, Applicants respectfully request that the Office reconsider and withdraw the rejection of claims 26-35 and 41-44 under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description.

B. Scope of Enablement

The Office maintains the rejection of claims 24-44 under 35 U.S.C. § 112, first paragraph, as lacking enablement for the full scope of the claims. (Final Office Action at page 3.) In particular, the Office states that the specification enables one to use the claimed oligonucleotides as antisense molecules for *in vitro* inhibition of expression of nucleic acids encoding SEQ ID NO:1. However, the Office asserts that, because no *in vivo* data is presented in the application, the application does not enable *in vivo* use of the claimed nucleotides, and thus does not enable methods of *in vivo* treating. Applicants respectfully traverse this rejection as it applies to rejected claims 26-35 and 41-44, and as it might be applied to new claims 45-63.

The present claims are directed to oligonucleotides, methods of making them, and an *in vitro* method of inhibiting expression of tenascin by a cell using the claimed oligonucleotides.

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The present specification specifically discloses the sequences of the claimed oligonucleotides. Synthesis of oligonucleotides was a routine matter for one of skill in the art at the time of this invention. Thus, there should be no question as to whether one of skill in the art would be able to make the presently claimed oligonucleotides. Further, the Office itself recognizes that one of skill in the art would know how to use the claimed oligonucleotides ("The instant disclosure is enabling for the scope drawn to the in vitro inhibition of expression of nucleic acids encoding human tenascin of SEQ ID NO:1 by the antisense claimed." (Final Office Action at Page 3.) Applicants submit that it is well established that a claimed product is enabled if one of skill in the art would know how to use it for any purpose. MPEP 2164.01(c) Thus, Applicants submit that the presently claimed oligonucleotides are enabled by the present specification.

The method of claim 63 recites the step of exposing a cell, *in vitro*, to an oligonucleotide according to the present claims. As discussed above, the Office itself recognizes that *in vitro* inhibition of expression of a tenascin comprising SEQ ID NO:1 is enabled. Applicants submit that it would not require undue or excessive experimentation to practice the full scope of the claimed method. That is, one of skill in the art could practice the claimed method on cells comprising any tenascin, not just one comprising SEQ ID NO:1.

To enable a claim, the specification must provide sufficient information for one of skill in the art to make and use the invention without undue experimentation. *In re Wands*, 858 F.2d, 731, 737 (Fed. Cir. 1988). As discussed above, the present specification teaches how to make the claimed oligonucleotides, and how to use them *in vitro* to inhibit expression of a tenascin comprising SEQ ID NO:1. Applicants submit that it would be a matter of routine experimentation to expose cells expressing any tenascin, *in vitro*, and determine whether the

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oligonucleotide used inhibited expression of the tenascin. Whether or not one of skill in the art could predict, *a priori*, which of the claimed oligonucleotides would inhibit which tenascin is not relevant to the question of enablement of claim 63. The relevant question is whether one of skill in the art would be able to inhibit expression of a chosen tenascin without undue experimentation, with the understanding that claims may encompass non-operative embodiments (*i.e.*, that not every claimed oligonucleotide will necessarily inhibit expression of every tenascin). Applicants submit that a person of skill in the art would, in fact, be able to do so simply by following the teachings of the present application, using any tenascin of interest. Thus, Applicants respectfully submit that claim 63 satisfies the enablement requirement of 35 U.S.C. § 112, first paragraph.

For at least the reasons set forth above and in previous responses, Applicants submit that the presently claimed invention is fully enabled by the specification. Therefore, Applicants request that the Office reconsider and withdraw the rejection of claims 26-35 and 41-44 as not enabled under 35 U.S.C. § 112, first paragraph.

II. *Rejections Under 35 U.S.C. § 103*

The Office maintains the rejection of claims 24-35 and 42 under 35 U.S.C. § 103 as obvious over Denner, Cleek (I), and Cleek (II) in view of Baracchini and Friesen. (Final Office Action at page 4.) Applicants traverse this rejection for the reasons of record, supplemented as follows.

Applicants submit that the Office has not set forth a *prima facie* case of obviousness because the references fail to teach or suggest all of the elements of the present claims. More

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particularly, the present claims recite specific oligonucleotides having defined sequences. In certain of the dependent claims, such as claims 32-34, the oligonucleotides have specific modifications. None of the references disclose or suggest the sequences recited in the present claims. The Office does not dispute this fact. Rather, in the Office Action dated April 24, 2001, at page 12, the Office concurs, stating "The primary references do not teach antisense oligonucleotides . . . including SEQ ID Nos:2-20 . . . nor do they teach all of the nucleobase and sugar modifications set forth in the claims including 3'-3' or 5'-5' inversions."

It appears that the Office is relying on the primary references to teach oligonucleotides. However, as admitted by the Office, these references, in fact, do not disclose the presently claimed oligonucleotides. Furthermore, the secondary references do not cure the deficiency of the primary references because they do not disclose or suggest the oligonucleotides of the present claims or the specific modifications recited in the claims. The secondary references merely provide a general teaching of various chemical modifications one can make to antisense oligonucleotides. A general incentive in the art, however, does not render obvious Applicants' specific invention. See, for example, *In re Deuel*, 34 USPQ2d 1210, 1216 (Fed. Cir. 1995). That is, a general incentive to modify the oligonucleotides of the primary references is not a teaching or suggestion of the specific oligonucleotides recited in the claims.

Because the cited references, alone or in combination, fail to disclose each and every element of the present claims, the Office has failed to set forth a *prima facie* case of obviousness. Accordingly, Applicants respectfully request that the Office withdraw the rejection of claims 26-35 and 42 under 35 U.S.C. § 103.

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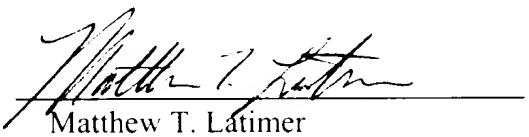
III. *Conclusion*

Applicants submit that this application is in condition for allowance. If, however, the Office believes anything else is necessary in order to place this application in even better condition for allowance, Applicants request that their undersigned representative be contacted at the telephone number or e-mail address listed below.

If there is any petition or fee due in connection with the filing of this Amendment that is not submitted herewith, please grant the petition and charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

By: 

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Date: January 30, 2003

Attachment:
Appendix

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**APPENDIX**
**(accompanying Amendment of January 30, 2003)**

**09/554,267**

IN THE CLAIMS:

Please amend claims 26, 27, 32, 33, and 42-44 as follows:

26. (Amended) [The] An oligonucleotide [according to claim 24, comprising] or physiologically tolerable salt thereof, comprising a sequence selected from[:]

SEQ[.] ID NO. 2[: 3'- GGTTTGGGTGGAGGTGG -5'],
SEQ[.] ID NO. 3[: 3'- GGAGGTGGTACCCCCGG -5'],
SEQ[.] ID NO. 4[: 3'- GGTGGTACCCCCGG -5'],
SEQ[.] ID NO. 5[: 3'- GGAGGTGGTACCCC -5'],
SEQ[.] ID NO. 6[: 3'- AGAAAGAACGAAAGGAA -5'],
SEQ[.] ID NO. 7[: 3'- GGAGGTGGTACC -5'],
SEQ[.] ID NO. 8[: 3'- GGAGCGATGGCTTCCA -5'],
SEQ[.] ID NO. 9[: 3'- AAAGGAACGGGAGCG -5'],
SEQ[.] ID NO. 10[: 3'- GGTCGGTTTGGGTGG -5'],
SEQ[.] ID NO. 11[: 3'- CTTACAGGTCCGTTGA -5'],
SEQ[.] ID NO. 12[: 3'- GGCCGTGTTCGCTGT -5'],
SEQ[.] ID NO. 13[: 3'- TCACCCCTCTTTCTGG -5'],
SEQ[.] ID NO. 14[: 3'- GGACACCGACACGG -5'],
SEQ[.] ID NO. 15[: 3'- AACGGGAGCGATGG -5'],
SEQ[.] ID NO. 16[: 3'- ATCTCGGGGTCGTC -5'],
SEQ[.] ID NO. 17[: 3'- AAAGAACGAAAGGAA -5'],
SEQ[.] ID NO. 19[: 3'- CCCGGTACTGA -5'], [or] and
SEQ[.] ID NO. 20[: 3'- CCACAGAAAGAAC -5'].

27. (Amended) [An] The oligonucleotide according to [any one of claims 24, 25, or 26] claim 26, wherein the oligonucleotide has one or more modifications.

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32. (Amended) The oligonucleotide according to claim 28, comprising a sequence selected from [the group consisting of:]

SEQ ID NO. 21[: 3'- GsGsTsTsTGGGTsGGAGGsTsGsG -5'],
SEQ ID NO. 22[. 3'- GsGsAsGGTsGGTsACsCCsCCsGsG -5'],
SEQ ID NO. 23[ 3'- GsGsTGGTsACsCsCCsCsGsG -5'],
SEQ ID NO. 24[: 3'- GsGsAGGTsGGTsACsCsCsC -5'],
SEQ ID NO. 25[: 3'- AsGsAAAGAAsCsGAAAGGsAsA -5'],
SEQ ID NO. 26[: 3'- GsGsAGGTsGGTsAsCsC -5'],
SEQ ID NO. 27[: 3'- GsGsAGCsGATsGGCsTsTsCsCsA -5'],
SEQ ID NO. 28[: 3'- AsAsAGGAACsGGGAGsCsG -5'],
SEQ ID NO. 29[: 3'- GsGsTCGGTsTsTGGGTsGsG -5'],
SEQ ID NO. 30[: 3'- CsTsTACAGGTsCsCGTsTsGsA -5'],
SEQ ID NO. 31[: 3'- GsGsCsCGsTGTsTCGCsTsGsT -5'],
SEQ ID NO. 32[: 3'- TsCsACsCCsCTsCsTTsTsCsTsGsG -5'],
SEQ ID NO. 33[: 3'- GsGsAsCACsCGACsACsGsG -5'],
SEQ ID NO. 34[: 3'- AsAsCsGGGAGCGATsGsG -5'],
SEQ ID NO. 35[: 3'- AsTsCsTCGGGGTsCsGsTsC -5'],
SEQ ID NO. 36[: 3'- AsAsAGAACsGAAAGGsAsA -5'],
SEQ ID NO. 37[: 3'- GsGsTGGTsACsCsCsC -5'],
SEQ ID NO. 38[: 3'- CsCsCsGGTsACsTsGsA -5'], and
SEQ ID NO. 39[: 3'- CsCsAsCAGAAAGsAsAsC -5'],

where "s" in the recited SEQ ID NOs. indicates the position of a modified internucleoside bridge.

33. (Amended) The oligonucleotide according to claim 28, comprising a sequence selected from[ the group consisting of:]

SEQ ID NO. 40[: 3'- GyGyTyTyTyGxGxGxTxGxGxAxGyGyTyGyG -5'],
SEQ ID NO. 41[: 3'- GyGyAyGyGyTxGxGxTxAxCxCxCyCyCyGyG -5'],
SEQ ID NO. 42[: 3'- GyGyTxGxGxTxAxCxCxCxCyCyGyG -5'],

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SEQ ID NO. 43[: 3'- GyGyAyGyGxTxGxGxTxAxCyCyCyC -5'],

SEQ ID NO. 44[: 3'- AyGyAyAxAxGxAxAxCxGxAxAxAyGyGyAyA -5'],

SEQ ID NO. 45[: 3'- GyGyAxGxGxTxGxGxTxAyCyC -5'],

SEQ ID NO. 46[: 3'- GyGyAxGxCxGxAxTxGyGyCyTyTyCyCyA -5'],

SEQ ID NO. 47[: 3'- AyAyAyGxGxAxAxCxGxGyGyAyGyCyG -5'],

SEQ ID NO. 48[: 3'- GyGyTyCxGxGxTxTxTxGxGyGyTyGyG -5'],

SEQ ID NO. 49[: 3'- CyTyTyAxCxAxGxGxTxCxCxGyTyTyGyA -5'],

SEQ ID NO. 50[: 3'- GyGyCyCxGxTxGxTxTxCxGyCyTyGyT -5'],

SEQ ID NO. 51[: 3'- TyCyAyCxCxCxCxTxCxTxTyTyCyTyGyG -5'],

SEQ ID NO. 52[: 3'- GyGyAyCxAxCxCxGxAxCxAyCyGyG -5'],

SEQ ID NO. 53[: 3'- AyAyCyGxGxGxAxGxCxGxAyTyGyG -5'],

SEQ ID NO. 54[: 3'- AyTyCyTxCxGxGxGxGxTxCxGyTyC -5'],

SEQ ID NO. 55[: 3'- AyAyAyGxAxAxCxGxAxAxAxGyGyAyA -5'],

SEQ ID NO. 56[: 3'- GyGyTxGxGxTxAxCxCyCyC -5'],

SEQ ID NO. 57[: 3'- CyCxCxGxGxTxAxCyTyGyA -5'], and

SEQ ID NO. 58[: 3'-CyCyAxCxAxGxAxAxAxGyAyAyC-5'],

where

"x" in the recited SEQ ID NOs., independently of one another, represents a phosphodiester internucleoside bridge or a modified internucleoside bridge, and

"y" in the recited SEQ ID NOs., independently of one another, represents the replacement of a sugar phosphate unit or of a β-D-2'-deoxyribose unit, the modified β-D-2'-deoxyribose unit being located at the 3'- end of "y".

42. (Amended) A process for the preparation of an oligonucleotide according to [any one of claims 24-26] claim 26, said process comprising synthesizing the oligonucleotide [being chemically synthesized] on a solid phase.

43. (Amended) A diagnostic comprising one or more oligonucleotides according to [any one of claims 24-26] claim 26.

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44. (Amended) A test kit comprising one or more oligonucleotides according [any one of claims 24-26] to claim 26.

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